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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,797	12/04/2001	John David Fraser	12669-002001/30072UPS00	9884

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EXAMINER	
JUEDES, AMY E	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
05/12/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

INFO@ORTPATENT.COM

Office Action Summary	Application No.	Applicant(s)	
	10/006,797	FRASER ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/27/08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6,10,11,13,15-18 and 21-45* is/are pending in the application.

4a) Of the above claim(s) *17,18,21-38 and 40-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-6, 10-11, 13, 15-16, and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 2/27/08, are acknowledged.

Claims 7-9 and 14 have been cancelled.
Claims 40-45 have been added.
Claims 5-6 have been amended.
Claims 2-6, 10-11, 13, 15-18, 21-45 are pending.

2. Claims 17-18 and 21-38 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. It is noted that new claims 40-45 (which correspond to previously withdrawn claims 7-9 and 14) are withdrawn from further consideration as being drawn to a non-elected species. In the reply to the restriction requirement filed on 12/9/04, Applicant elected SPE-C as the specific species of targeting molecule. Thus, the other specific variants of SPE-C recited in claims 40-45 are non-elected species.

Claims 2-6, 10-11, 13, 15-16, and 39 are being acted upon.

3. The rejection of the claims under 35 U.S.C. 103 is withdrawn in view of Applicant's remarks. Applicant argues that the claimed conjugates possess the unexpected property of inducing an enhanced immune response to the antigen component. Based on the teachings of McCormick et al. and the '964 patent, the ordinary artisan would not have expected to obtain an enhanced immune response to the plasma protein (i.e., the antigen).

4. The rejection of claims 5-6 under 35 U.S.C. 112 first paragraph for the recitation of a superantigen "derived from" *Staphylococcus aureus* or *Streptococcus pyogenes* is withdrawn in view of Applicant's amendment to the claims.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 2—6, 10-11, 13, 15-16, and 39 stand rejected under 35 U.S.C. 112, first paragraph, as the specification does not

contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) An immunomodulator comprising a targeting molecule that "includes a Class II MHC binding site" and a T cell receptor binding site of a superantigen, the T binding site having one or more mutations that "reduce its T cell proliferation activity"

B) An immunomodulator wherein the mutated T cell receptor binding site "reduces the T cell proliferation activity to equal to or greater than 10,0000 fold"

Applicant indicates that support for the limitations of claim 2 can be found on page 3 of the specification, and support for new claim 39 can be found in Table 3 at page 21 of the specification.

A review of the specification fails to reveal support for the new limitation.

Regarding A), the instant specification discloses on pg. 3 a targeting molecule that mimics a superantigen but does not include a fully functional T-cell receptor binding site and a targeting molecule which is structurally a superantigen but for a disrupted T-cell receptor binding site. However, there is no disclosure of a targeting molecule that specifically "includes a class II binding site", as now claimed. Furthermore, the targeting molecules disclosed on page 3 include those without a fully functional T cell receptor binding site, or those that have little or no ability to activate T cells. However, these generic disclosures are not adequate to support claims which specifically recite that the T cell binding site "reduces T cell proliferation activity".

Regarding B), the instant specification on page 21 discloses specific targeting molecules such as SMEZ-2 W75L that reduce T cell proliferation to greater than 10,000 fold. However, this specific example is not adequate to support the more generic claims of the instant application which are drawn to an immunomodulator comprising any superantigen with any mutation in the T cell binding site.

Applicant's arguments filed 2/27/08 have been fully considered, but they are not persuasive.

Regarding A), Applicant argues that the specification discloses an APC targeting molecule that mimics a superantigen but does not include a fully functional T cell receptor binding site, and a molecule that is structurally a superantigen but for a disrupted T cell binding site (i.e. superantigen mutants containing mutations only in the T cell binding domain). Applicant argues that it is well known that superantigens comprise MHC class II binding sites, and thus the skilled artisan would readily know that the APC-targeting molecules included in the claimed conjugates comprise an MHC binding site.

The instant claims are drawn to an APC targeting molecule which "includes a Class II MHC binding site and a T cell receptor binding site of a superantigen", wherein the T cell binding site comprises one or more mutations. However, the claims do not require that the only mutations be in the TCR binding site. For example, since the MHC binding domain of most superantigens is located at the N-terminus, the claims might encompass APC targeting molecules that have mutations or deletions in the C terminus, outside of the MHC or T cell binding sites (i.e. a superantigen which "includes a Class II binding site"). Applicant concedes that the APC targeting molecules disclosed by the specification are intended to encompass superantigen mutants containing mutations **only** in the T cell binding domain. Additionally, all of the examples disclosed by the specification involve superantigens comprising mutations **only** to the TCR binding site. However, the instant claims have a much broader scope than what is disclosed in the specification. For example, the claims might encompass an APC targeting molecule comprising only a minimal MHC binding site, but lacking other portions of the C-terminus of the superantigen that are not involved in MHC binding.

Applicant further argues that "T cell activating activity" and "T cell proliferation activity" are synonymous to a person skilled in the art, since it is well known that activated T cells undergo proliferation. The specification discloses targeting molecules with little or no ability to activate T cells. The term "T cell activity" refers to a genus of activities, including proliferation, cytokine production, chemokine production, upregulation of activation markers, etc. The generic disclosure of a T cell "activity" does not provide adequate support for the specific activity of T cell proliferation.

Regarding B), Applicant argues that the specification teaches on page 3 superantigen mutations with no ability to activate T cells, and the specification discloses on page 16 that a fully ablated TCR binding superantigen (i.e. having no ability to activate T cells) is defined as one that displays less than about 0.0001% of proliferative activity of the WT superantigen.

The disclosure of a TCR binding mutant with a 1 million fold reduction in activity does not provide adequate support for the instant claims which are drawn to a mutant which reduces the

activity to equal to or greater than 10,000 fold compared to WT.

7. Claims 2-6, 10-11, 13, 15-16, and 39 stand rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A conjugate that "binds to a Class II MHC molecule" (Claim 2, and dependant claims 3-6, 10-11, 13, 15-16, and 39).

Applicant indicates that support for the new limitations of the claims can be found on page 15 and 22 of the specification.

A review of the specification fails to reveal support for the new limitations.

At page 22, the specification discloses a specific example of testing in vivo T cell response to a particular superantigen construct. However, there is no disclosure of a conjugate that "binds to a Class II MHC molecule". Page 15 of the specification discloses a specific example of generating specific SPEC mutants and testing the mutants for their ability to bind to MHC class II. However, the disclosure of a specific example of testing mutants of SPEC for their ability to bind MHC does not provide adequate support for superantigen "conjugates" that bind to MHC, as now claimed.

Applicant's arguments filed 2/27/08 have been fully considered, but they are not persuasive.

Applicant argues that the disclosure of a targeting molecule that is structurally a superantigen but for a disrupted TCR binding site would necessarily comprise a MHC class II binding site. However, whether a targeting molecule that is structurally a superantigen would comprise an MHC binding site is irrelevant, since the instant claims recite that the "conjugate" binds to Class II MHC. The specification does not disclose that the "conjugate" binds to MHC molecules.

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this

action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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